Assessing Neurodevelopmental outcome in children with hydrocephalus in Malawi. A Pilot Study

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Abstract

Introduction

Congenital and infantile hydrocephalus are assumed to be major contributors to pediatric morbidity, mortality and functional disability in low-income countries. Despite this, epidemiologic data and the overview of neurodevelopmental outcomes in these regions is very limited. We aimed to pilot the use of a wide range of more locally suitable tools to assess neurodevelopment to understand whether they were feasible for use and could provide estimates of developmental delay and poor functioning in a population of children with hydrocephalus in Malawi.

Methods

We conducted a prospective observational cohort study, at the tertiary neurosurgery clinic in Blantyre, Malawi in 2018, recruiting consecutive children with congenital and infantile hydrocephalus who were previously treated with ventriculoperitoneal shunts and endoscopic third ventriculostomy (ETV) in the neurosurgery unit of the hospital. We assessed demographic details, and gained information on children’s functioning using the Liverpool Outcome Score (LOS), and the Eating and Drinking Ability Classification System as well as full anthropometric assessment and child development with the Malawi Developmental Assessment Tool (MDAT).

Results

All tools were feasible for use, easy to train on, could be used for assessing children with hydrocephalus and were suitable to adapt for our environment. We evaluated 41 children, aged 2 to 60 months with a mean age of 22.6 months (interquartile range [IQR] = 8.3 months -36.5 months). Functional assessment using the Liverpool Outcome Score showed the majority of children 92.7% (CI 80.1- 98.5, n=38) had severe sequelae from the hydrocephalus and were dependent on their parents or caregivers. Only 27 children (65.9%, CI 49.4, 80.0) had full or expected control of their bowel and bladder and 6 children (14.6%, CI 5.6, 29.2), had a recent history of seizures. About two thirds (63.4% CI 45.0-77.9, n=26/41) of children were able to eat and to drink safely and efficiently. Over two thirds of the children (70.7%, CI 56.8, 84.6, n=29) were stunted and almost half of the cohort underweight (43.9% ,(CI 28.5, 60.3, n=18). Almost half 48.8% (CI 32.9, 64.9, n=20/41) had developmental delay on MDAT with 41.5% (CI 26.4, 56.6, n=17/41) graded as severely delayed (-<2sd on developmental age z score). We found significant associations between dependence identified by the LOS and developmental delay according to the MDAT (p=0.014, Pearson’s chi-squared test).

Conclusion

This pilot study demonstrates that the assessment tools we used identified a high proportion of children with hydrocephalus as having functional difficulties, stunted growth and developmental delay, in Malawi. Use of these tools can now be scaled up and will be helpful to support research in understanding what factors contribute to poor functioning, growth and development in these cohorts and help us to investigate what strategies may prevent and support children with hydrocephalus in African settings.

Introduction:

Hydrocephalus and spina bifida are thought to be common among children in low-income countries, however empirical data from these settings is extremely poor.[1] It is estimated that approximately 1.45 per 1000 children in Africa develop hydrocephalus.[1] however these studies are very varied due to difficulties in consensus on definitions and use of similar epidemiological methods. Currently, epidemiologic and neurodevelopmental data from low income countries, such as Malawi, are truly lacking with only one report from Malawi providing rates of hydrocephalus at birth of 0.23/1000 – much lower than estimates for Africa as a whole.[2] This low rate is likely due to exclusion of children who developed hydrocephalus after birth and it is likely that Malawi has higher rates, and rates similar to those in other African countries.[3,4] We know that children in high income settings with hydrocephalus have high levels of morbidity, mortality and functional disability. Itis likely that these rates are even higher in low and middle income settings.[3,5,6] One prospective study from Lilongwe in Malawi demonstrated high rates of mortality (32%) of those children identified and followed up at 3 months however this study did not extend beyond this.[7] The current lack of data from Malawi, as well as elsewhere in Africa, leads to difficulties in advocating for better preventative care but also for providing clear local treatment recommendations and guidelines.

The main focus of this study was to understand whether tools to assess functioning and development of children in Malawi could identify difficulties in a population of children with hydrocephalus up to 5 years of age and could estimate rates of difficulties in those children who had hydrocephalus treated with ventriculoperitoneal shunting and endoscopic third ventriculostomy (ETV) at a tertiary clinic in Malawi.[8]

Methods:

Setting and subjects:

We performed a prospective observational cohort study between April and July 2018 recruiting children with hydrocephalus in Malawi seen in our clinic. The neurosurgical department of Queen Elizabeth Central Hospital (QECH) in the southern city of Blantyre was the only comprehensive (specialist) neurosurgical unit in the country at the time the study was conducted.[8]

Recruitment:

We aimed to recruit consecutive children who were seen in the once weekly neurosurgical clinics over a period of 12 weeks. We approached caregivers of any child seen in the clinic who were between 0 and 5 years and previously treated for a primary diagnosis of hydrocephalus (which was defined as progressive enlargement of the child’s head due to cerebrospinal fluid accumulation as a result of a hydrodynamic disorder (i.e. pressure-driven) of cerebrospinal fluid circulation within the brain).[8] In our setting a diagnosis of hydrocephalus is made from clinical history of head enlargement and poor progression of child developmental milestones, enlarged head circumference using a tape measure and the WHO head circumference standardized chart, and ultrasound scanning through the fontanelle in children with an open fontanelle. At the time of the study, our hospital did not have a computed tomography scanner. Those with closed fontanelle where trans-fontanellar ultrasonography could not have been done, were radiologically investigated with 0.3 Tesla magnetic resonance scanner by General Electric. All children underwent flexible endoscopy and endoscopic third ventriculostomy was attempted. Where endoscopic third ventriculostomy could not have been done, a ventriculoperitoneal shunt (Chabbra, India) was inserted. The children stayed in hospital for about a week after surgery and then discharged and followed up periodically in the neurosurgery outpatient clinic. For this study, all children treated for hydrocephalus between April 2013 and April 2018, who presented for the neurosurgery outpatient clinic were enrolled. All caregivers were asked to return with the children for a full neurodevelopmental assessment if they consented to take part in the study. Some caregivers were contacted by telephone to encourage them to come with their children to the clinic for assessment.

Assessments:

We completed questionnaires with all consenting caregivers as well as neurodevelopmental assessments on all children. Questionnaires included information on socioeconomic status, maternal education and household situation (Demographic and Health Survey (DHS)) as well as the Liverpool Outcome Score (LOS) and the Eating and Drinking Ability Classification System (EDACS).[9–12] We then proceeded with direct assessments of the children through anthropometric measurements and the Malawi Developmental Assessment Tool (MDAT).[13]

LOS assesses basic motor and self-care skills, as well as simple cognitive and behavioral functions, through a series of 10 questions posed to the parent or caregiver, and five observations of the child performing simple activities.[14] Examples of questions include those looking at; speech and communication, feeding ability, changes in behavior, performance at school, work, or in routine activities at home and occurrence of seizures. For many questions, the interviewee is asked to compare the child’s ability with his or her peers of similar age in the community.

EDACS was created to describe the full range of eating and drinking ability of children and young people with cerebral palsy in five distinct levels, using key features of safety and efficiency.[11,15–17] EDACS focuses on a child's usual performance of biting, chewing, drinking, and swallowing and the coordination of these with respiration. Descriptions of different levels of ability include details of food and fluid textures that can be managed without choking or aspiration. Descriptions also include the extent to which food and fluid are retained in the mouth and the speed and range of movement brought to the task. Like the Gross Motor Function Classification System (GMFCS) EDACS has been shown to be valid for children and young people with cerebral palsy.[16]

Anthropometric assessments were conducted according to the WHO guidelines.[18,19] Weight was recorded using a SECA weighing scale, length using a flat stadiometer (for all children under the age of 2 and those who could not stand) and height was measured using the same stadiometer. These were repeated three times with the most common or middle measurement taken each time.[18,19] Head circumference was measured using a measuring tape passed around the widest circumference of the head, usually just above the eyebrows and passing above the occipital protuberance.[20] Again, measurements were repeated three times and the most common or middle measurement recorded.

The MDAT was initially developed and validated in Malawi, and has been found to be sensitive in assessing neurodevelopment in such settings. The tool measures gross motor, fine motor, speech and language, and social behavior. It has been used now in over 25 countries and has been well validated to assess child development in Sub-Saharan Africa.[21]

All tools were translated and back translated into Chichewa. The participants were primarily assessed by two local research assistants. Prior to data collection the researchers all received training on the use of the LOS and EDACS, and on the MDAT by an experienced MDAT practitioner. They also received training on anthropometric assessment and were assessed to be reliable, with a high inter-rater reliability, prior to commencing the study. The training for all tools was conducted over 5 days.

Participants were provided with an anonymized identification code, and data was coded onto the assessment sheets at the time of data collection to maximize confidentiality.

Scoring and Analysis:

The Liverpool outcome score was graded on a one to five Likert scale for all 15 questions. The final score is the lowest number that was scored for any of the questions.[10] Children were classified as “dependent” if their final outcomes score was as low as two.

Anthropometric measurements were converted into z-scores for age using Anthrostat.[18]

As for the MDAT score, the gross motor, fine motor and language domains are assessed by directly observing the child while the social domain is assessed by directing questions to the caregiver. It is a 136-item tool with 34 items in each developmental domain. The assessor scores items as “pass” or “fail” and if the child is uncooperative or unwell the score is recorded as “don’t know”. [21] The overall score for each domain was remarked “normal” if the child has passed all items in accordance to their age and a remark of “delayed” if has failed 3 or more items.

Statistical analysis was performed using SPSS 26.0 (Lead Technologies, INC, Charlotte, USA). The explorative level of significance was set on p<0.05.”

Ethics:

The study complied with the 1996 ICH GCP guidelines and 2000 Declaration of Helsinki and was approved by the ethics committee at the Liverpool School of Tropical Medicine (Protocol M1823), in the United Kingdom, and the College of Medicine Research and Ethics Committee (Protocol P.03/18/2376), in Malawi.[22] Valid written informed consent was obtained from accompanying parents before the assessments took place. Written consent took the form of a signature or an inked thumbprint if the parents could not write.

Results:

Patient and family characteristics:

From 51 included participants, 41 were enrolled in final analysis. The10 patients were excluded due to incomplete MDAT data or missing date of birth.

Table 1 provides descriptive information about the population of children analysed. The age of the children ranged from 2 to 60 months with a mean age of 22.6 months (interquartile range [IQR] = 8.3 months -36.5 months). The majority of participants were male 61% (CI 44.5,75.8, n=25). Most families 46% (CI 31.0, 61.6, n=19) came from peri-urban Blantyre Thirteen (13) families (32%, CI 18.1,48.1) lived in a rural location whilst a further eight (19.5%, CI 8.8, 34.9) lived in a remote location. Over half, 56.1% (39.8, 71.5, n=23) of mothers had attended primary school.

Functional disability score:

Table 1 shows that the majority of children in our cohort 92.7% (CI 80.1- 98.5, n=38) had severe sequelae according to the Liverpool Outcome Score and were found to be dependent on their parents or caregivers. Only 3 children’s caregivers (7.3%, CI 0.0, 15.3) reported no problems and moderate sequelae were only documented in 9 children (22%, CI 9.3, 34.7, table 1). A total of 27 children (65.9%, CI 49.4, 80.0) had full or expected control of their bowel and bladder. Incontinence affected 13 children (31.7%, CI 18.1, 48.1) and only one child (2.4%, CI 0.1, 12.7) needed more help than would be expected from a child with the same age. Six children (14.6%, CI 5.6, 29.2), were reported to have had a seizure within the preceding two months and none of the children with seizures were taking any anti-epileptic medication.

We found significant associations between dependence identified by the LOS and developmental delay according to the MDAT (p=0.014, Pearson’s chi-squared test).

Eating and Drinking Function:

A total of 63.4% (CI 45.0,77.9, n=26/41) of children were able to eat and to drink safely and efficiently, while 9.8% (CI 2.7, 23.1, n=4/41) of children were reported by their parents to be able to drink and to eat but with some limitations in efficiency. Only 26.8% (CI 14.2, 42.9, n=11/41) of children had limitations to safety when eating and drinking. None of the children in the cohort were reported to be unable to feed or drink so as to require alternative methods of nutritional intake such as tube feeding, although it should be clear that tube feeding is not presently an option in Malawi.

Anthropometry:

The mean WAZ of children in our study was -1.55 (SD 3.09), with a mean HAZ of -7.43 (SD 7.54) and a mean HCAZ of 5.11 (SD 4.55). Stunted growth (growth <-2SD below the norm) was documented in 70.7% (CI 56.8, 84.6, n=29) of the children and almost half of the examined cohort, was underweight 43.9% (CI 28.5, 60.3, n=18).

Developmental scores:

Table 1 shows that about half the children (n= 20/41, 48.8%, CI 32.9, 64.9) had neurodevelopmental delays using the MDAT. We segregate the performance of the children according to the different domains assessed by the MDAT (table 1). Motor function was the most often delayed on the MDAT tool with 70.0% (CI 44.5, 75.8, n=25) of children being delayed in gross motor skills and 58.5% (CI 42.1, 73.7, n=24) in fine motor skills. 46.3% of children were delayed in their adaptive social skills (CI 31, 61.6, n=19). In all these three domains, the majority of the children had severe developmental difficulties. In the language domain of the MDAT, most of the children performed well, with only 26.8% (CI 14.2, 42.9, n=11) experiencing delays. The proportion of children with severe language development was significantly lower than the proportion of children with severe delays in gross motor, fine motor and social development.

Discussion:

We aimed to evaluate the neurodevelopmental and functional outcomes of children with hydrocephalus treated at tertiary hospital in Malawi. Although this study was small and exploratory, it is one of the first studies which has provided information on developmental attainment and functioning of children with hydrocephalus in an African setting using a wide battery of assessment tools which look both at functioning and developmental attainment in young children. Our results demonstrate a high level of functional difficulties as well as severe developmental delay in our cohort of children seen in the tertiary clinic at QECH. Numbers of children identified as having difficulties varied with the assessment tool. Surprisingly, very few other studies have studied the neurodevelopment of children with hydrocephalus. The study conducted in Turkey, using the Denver Developmental Screening Tool (DDST), demonstrated even higher rates of developmental delay than our study.[6] In the Turkish study, 70.8% of their cohort of children with hydrocephalus treated with ventriculoperitoneal shunts having delayed development.[23] Subgroups of children with hydrocephalus were evaluated in the study from Turkey, such as those with congenital macrocephaly, microcephaly or spina bifida. These were not possible to outline in our Malawian cohort due to our smaller numbers. It is clear that in our specific cohort of children fully tested in Malawi, we have high rates of severe developmental delay, however it is unclear as to how much our rates are specific to the population of children seen in our clinic. To delineate this better, we would need a much larger representative population of children with this condition in Malawi. Despite this, our study has now provided us with knowledge as to the utility of the tools chosen to measure outcomes in these populations. With this in mind we can now be confident that our assessment tools are able to identify developmental delay and functional disabilities in children with hydrocephalus in Africa and can now be used beyond this pilot study in any larger research studies which may consider looking at neurodevelopmental outcomes dependent on timing and, types of treatments provided as well as aetiology of the condition.

Our sample has identified only 6 children with seizures. None of these children have been treated with anticonvulsants. It is clear that all children with hydrocephalus should be assessed for seizures during follow up in the clinics. Parents may not be reporting these and it is likely that the numbers of children with hydrocephalus developing epilepsy are higher than we thought.[24]

Children with hydrocephalus often have higher levels of malnutrition compared to the national average.[25] This is mirrored in our study where we identified 70.7% (CI 56.8, 84.6) of the children with hydrocephalus in our cohort as having stunted growth and half being underweight (43.9%, CI 28.5, 60.3). It is clear that we should ensure that we consider nutritional status within the specific cohorts of children with hydrocephalus that we see and ensure that it is assessed.[26] We do know that the true measurement of growth in children with hydrocephalus may be more difficult due to their disability.[27] Despite this, researchers would now advocate using a range of measures such as skinfold thickness or arm span. These were not possible to do in our study but should be done in the future and arm span could even be better used in clinical settings. Although the rates of children with malnutrition and stunting are improving in Malawi (according to the Malawi National Demographic and Health Survey 2017), children with hydrocephalus in Malawi are likely to be more at risk. Our study is the first study, to our knowledge, that has measured eating and drinking abilities in children with hydrocephalus using a standardized tool in a low or middle income country. In using this, we found that a proportion of these children had difficulties with eating and drinking according to the eating and drinking. Furthermore, many studies have clearly demonstrated the close linkages between stunting and performance on developmental assessment.[21,28] It is therefore possible that malnutrition could also further be contributing to the developmental delay in our children with hydrocephalus It may be that some of these children may benefit from earlier nutritional support and intervention in the way of supplementation or in the future, with improvements in technology and systems, maybe we could consider enteral feeding. This is presently not possible in Malawi. It is clear that assessment of nutrition in children with hydrocephalus is vital and can provide evidence for nutritional interventions for children in clinics.[29] Further studies should always ensure that anthropometrics are conducted using arm span or tibial length.[30]

Limitations:

Our study was limited by several factors. Firstly, our sample size was relatively small, was a sample of children from a specific tertiary clinic and the participants were only assessed over a period of time. Secondly, participants were recruited opportunistically likely to mean that we had more children with certain types of hydrocephalus, those from certain socio-demographic situations and those who were seeking treatment. It may be that those in more rural areas or those with milder forms of the disease did not attend our service and we therefore would have less information about these children.

Although we conducted anthropometry on the children, it is difficult to know how accurate this was, particularly as more specific ways of assessing anthropometry and body composition, useful for children with disabilities, were not utilized in our study. Although we found differences in three domains of the MDAT, the social domain may have been more unreliable and may have been more biased particularly as this is parent reported rather than direct assessment. We had little clinical information on the aetiology and all the clinical features of the children with hydrocephalus who were included in the study. It may be the case that children with different aetiologies and disease types have different prognostic expectations which could not have been differentiated in our study. Further large studies will be necessary to confirm our results and based on that identify further risk factors for neurodevelopmental delay and improve treatment guidelines adapted for the region of Malawi.

Conclusion:

Our study demonstrates that a high proportion of children suffering from hydrocephalus have marked developmental delay and functional difficulties as well as stunted growth and are underweight. This study demonstrates our ability to identify children with difficulties, use these measures for follow up and use them for larger trials and studies which could be undertaken to understand the effect of interventions and early identification on supporting and treating these children to enable them to thrive better. Further prospective studies are needed in order to define the risk factors and treatment protocols of children with hydrocephalus in Malawi.

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